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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/755,325	01/05/2001	Ali Hemmati-Brivanlou	7529/1H460US2	7033

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EXAMINER
ZEMAN, ROBERT A

ART UNIT	PAPER NUMBER
1645	10

DATE MAILED: 02/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/755,325	HEMMATI-BRIVANLOU ET AL.	
	Examiner	Art Unit	
	Robert A. Zeman	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 November 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-26* is/are pending in the application.

4a) Of the above claim(s) *20-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5 .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

- [X] 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).
- [ ] 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).
- [ ] 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).
- [ ] 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."
- [ ] 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).
- [ ] 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).
- [X] 7. Other: the drawings contain sequences with the requisite SEQ ID identifiers.

Applicant Must Provide:

- [ ] An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".
- [ ] An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.
- [ ] A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
For CRF Submission Help, call (703) 308-4212
PatentIn Software Program Support
Technical Assistance.....703-287-0200
To Purchase PatentIn Software.....703-306-2600

PLEASE RETURN A COPY OF THIS NOTICE WITH YOUR REPLY

DETAILED ACTION

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. §1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. §§1.821-1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements for Patent Applications Containing Nucleotide Sequence and/or Amino Acid Sequence Disclosures. Any questions regarding compliance with the sequence rules requirements specifically should be directed to the departments listed at the bottom of the Notice to Comply. Applicant is requested to return a copy of the attached Notice to Comply with their response. Applicant is given the same period in which to comply with the sequence rules as is available to reply to this action.

Election/Restrictions

Applicant's election with traverse of Group I in Paper No. 8 is acknowledged. The traversal is on the ground(s) that the designated groups of claims do not define products and methods for using such products are distinct or which warrant separate examination and searches. This is not found persuasive because the searches of the various groups outlined in the restriction requirement would not be coextensive in scope.

The requirement is still deemed proper and is therefore made FINAL.

Claims 13-26 are pending. Claims 20-26 have been withdrawn from consideration. Claims 13-19 are currently under examination.

35 U.S.C. First Paragraph, Enablement Rejection

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 13-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for polypeptides having a sequence comprising SEQ ID NO:2 or SEQ ID NO:4, does not reasonably provide enablement for the myriads of other polypeptides species claimed. The specification is enabling only for claims limited to polypeptides represented by SEQ ID NO:2 or 4 because the specification does not reasonably provide enablement for polypeptide variants having substantial homology to SEQ ID NO:2. The specification does not enable any person skilled in the art to which it pertains or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims.

Claims 13-16 and 19 are drawn to isolated eIF-4AIII proteins with substantial homology to the amino acid sequence recited in SEQ ID NO:2. Said polypeptides have no claimed biochemical, immunological or physiological function. Claims 17 and 18 are drawn to isolated proteolytic eIF-4AIII protein fragments with substantial homology to the amino acid sequence recited in SEQ ID NO:2. The specification defines substantial homology as "having at least about 80% of amino acids that are either identical or contain conservative amino acid changes over the defined length o f the polypeptide sequences".

Protein chemistry is probably one of the most unpredictable areas of biotechnology Consequently, the effects of sequence dissimilarities upon protein structure and function cannot be predicted. Bowie et al (Science, 1990, 257:1306-1310) teach that an amino acid sequence encodes a

message that determines the shape and function of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function and carry out the instructions of the genome and further teaches that the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. (column 1, page 1306). Bowie et al further teach that while it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (column 2, page 1306). The sensitivity of proteins to alterations of even a single amino acid in a sequence are exemplified by Burgess et al (J. of Cell Bio. 111:2129-2138, 1990) who teach that replacement of a single lysine reside at position 118 of acidic fibroblast growth factor by glutamic acid led to the substantial loss of heparin binding, receptor binding and biological activity of the protein and by Lazar et al. (Molecular and Cellular Biology, 1988, 8:1247-1252) who teach that in transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen. These references demonstrate that even a single amino acid substitution will often dramatically affect the biological activity and characteristics of a protein. Clearly, proteins with up to 20% dissimilarity, to the polypeptides of SEQ ID NO:2 that maintained the characteristics of the polypeptides encoded by SEQ ID NO:2 could not be predicted. Additionally, Bork (Genome Research, 2000,10:398-400) clearly teaches the pitfalls associated with comparative sequence analysis for predicting protein function because of the known error margins for high-throughput computational methods. Bork specifically teaches that computational sequence analysis is far from perfect,

despite the fact that sequencing itself is highly automated and accurate (p. 398, column 1). One of the reasons for the inaccuracy is that the quality of data in public sequence databases is still insufficient. This is particularly true for data on protein function. Protein function is context dependent, and both molecular and cellular aspects have to be considered (p. 398, column 2). Conclusions from the comparison analysis are often stretched with regard to protein products (p. 398, column 3). Further, although gene annotation via sequence database searches is already a routine job, even here the error rate is considerable (p. 399, column 2). Most features predicted with an accuracy of greater than 70% are of structural nature and, at best, only indirectly imply a certain functionality (see legend for table 1, page 399). As more sequences are added and as errors accumulate and propagate it becomes more difficult to infer correct function from the many possibilities revealed by database search (p. 399, paragraph bridging columns 2 and 3). The reference finally cautions that although the current methods seem to capture important features and explain general trends, 30% of those features are missing or predicted wrongly. This has to be kept in mind when processing the results further (p. 400, paragraph bridging cols 1 and 2). Clearly, given not only the teachings of Bowie et al., Lazar et al. and Burgess et al. but also the limitations and pitfalls of using computational sequence analysis and the unknown effects of alternative splicing, post translational modification and cellular context on protein function as taught by Bork, the claimed proteins could not be predicted based on sequence identity to SEQ ID NO:2. Further, even if a given polypeptide possesses all the structural limitations of the claimed invention, neither the specification nor any art of record teaches what that polypeptide is, what it does, does not teach a relationship to any specific disease or establish any involvement of the polypeptide in the etiology of any specific disease or teach which fragments might be active or which derivatives would function as claimed. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth, and it cannot be predicted from the disclosure how to make/use polypeptides with

substantial homology to SEQ ID NO:2. In view of the above, one of skill in the art would be forced into undue experimentation to practice the claimed invention.

35 U.S.C. 112, Written Description Rejection

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, first paragraph "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Claims 13-19 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, hid possession of the claimed invention.

The specification discloses SEQ ID NO:2 and SEQ ID NO:4 that corresponds isolated eIF-4AIII proteins (or a portion thereof). SEQ ID NO: 2 and 4 meet the written description provision of 35 USC 112, first paragraph. However, the aforementioned claims are directed to encompass, sequences that have at least 80% identity (substantial homology) to SEQ ID NO:2, corresponding sequences from other species, mutated sequences. allelic variants, splice variants, sequences that have a recited degree of identity (similarity. homology), and so forth. None of these sequences meet the written description provision of 35 USC 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by the claim.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed."* (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of SEQ ID NO:2 and 4, the skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptides and/or proteins, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The polypeptide itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

> Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404. 1405 held that: ...To fulfill the written description requirement, a patent specification must describe an invention and does so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines. Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood,* 107 F.3d at 1572, 41 USPQ2datl966.
>
> An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. *Fiers v. Revel,* 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.
>
> The name cDNA is not itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA. Describing a method of preparing a cDNA or even describing the protein that the cDNA encodes, as the example does, does not necessarily describe the cDNA itself. No sequence information indicating which nucleotides constitute human cDNA

appears in the patent, as appears for rat cDNA in Example 5 of the patent. Accordingly, the specification does not provide a written description of the invention of claim 5.

Therefore, only SEQ ID NO: 2 and 4, but not the full breadth of the claims meet the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

Additionally, It is noted that applicant(s) have listed a sequence which is known in the prior art and which has a high percentage sequence similarity to a claimed sequence. Absent factual evidence, a percentage sequence similarity of less than 100 % is not deemed to reasonably support to one skilled in the art whether the biochemical activity of the claimed subject matter would be the same as that of such a similar known biomolecule. It is known for nucleic acids as well as proteins, for example, that even a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many instances, albeit not in all cases. The effects of these changes are largely unpredictable as to which ones have a significant effect versus not. Therefore, the citation of sequence similarity results in an unpredictable and therefore unreliable correspondence between the claimed biomolecule and the indicated similar biomolecule of known function and therefore lacks support regarding utility and/or enablement. Several publications document this unpredictability of the relationship between sequence and function, albeit that certain specific sequences may be found to be conserved over biomolecules of related function upon a significant amount of further research. See the following publications that support this unpredictability as well as noting certain conserved sequences in limited specific cases.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 13-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 13 and 19 are rendered vague and indefinite by the use of the term "substantially homologous". It is unclear what is meant by said term. The specification defines "substantial homology" as "having at least about 80% of amino acids that are either identical or contain conservative amino acid changes over the defined length of the polypeptide sequences". However, this definition is itself vague and indefinite since it does not explicitly disclose what constitutes a conservative amino acid change. As written, it is impossible to determine the metes and bounds of the claimed invention.

Claim 14 is rendered vague and indefinite by the use of the term "conservative substitution" It is unclear what amino acid substitutions are deemed by Applicant to be "conservative".

Claim 15 is rendered vague and indefinite by the use of the phrase "containing the amino acid sequence of SEQ ID NO:4". Is Applicant claiming that the sequence of said protein comprises SEQ ID NO:4 or that another protein with the sequence of SEQ ID NO:4 is associated with the claimed protein? As written, it is impossible to determine the metes and bounds of the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The instant invention is drawn to isolated eIF-4AIII proteins with an amino acid sequence substantially homologous to SEQ ID NO:2 and proteolytic fragments thereof.

Claims 13-14 and 17 are rejected under 35 U.S.C. 102(a) as being anticipated by Weinstein et al. (Development Vol. 124. pages 4235-4242, 1997).

Weinstein et al. disclose isolated eIF-4AIII proteins with an amino acid sequence substantially homologous to SEQ ID NO:2 (see page 4236, column 2 and Figure 1). With regard to claim 17, while the proteolytic activity of said proteins (fragments) was not explicitly disclosed, said activity is, absent of evidence to the contrary, an inherent property of the protein (fragment). Moreover, the disclosed protein constitutes a fragment (414 amino acids) of the protein of SEQ ID NO:2 (415 amino acids).

Claims 13-14 and 17are rejected under 35 U.S.C. 102(b) as being anticipated by Leffers et al. (EMBL Accession Number S45142, January, 13, 1995).

Leffers et al. disclose an isolated protein with an amino acid sequence substantially homologous to SEQ ID NO:2 (see page attached STIC search report). With regard to claim 17, while the proteolytic activity of said proteins (fragments) was not explicitly disclosed, said activity is, absent of evidence to the contrary, an inherent property of the protein (fragment). Moreover, the disclosed protein constitutes a fragment (411 amino acids) of the protein of SEQ ID NO:2 (415 amino acids).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The instant invention is drawn to isolated eIF-4AIII proteins with an amino acid sequence substantially homologous to SEQ ID NO:2, proteolytic fragments thereof and fusion proteins thereof.

Claims 13, 15-16 and 18-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weinstein et al. (Development Vol. 124. pages 4235-4242, 1997).

Weinstein et al. disclose isolated eIF-4AIII proteins with an amino acid sequence substantially homologous to SEQ ID NO:2 (see page 4236, column 2 and Figure 1). With regard to claim 17, while the proteolytic activity of said proteins (fragments) was not explicitly disclosed, said activity is, absent of evidence to the contrary, an inherent property of the protein (fragment). Moreover, the disclosed protein constitutes a fragment (414 amino acids) of the protein of SEQ ID NO:2 (415 amino acids).Weinstein et al. differs from the instant invention in that they don't explicitly disclose the use of said proteins and protein fragments in fusion (chimeric) proteins nor do they disclose an isolated eIF-4AIII protein containing SEQ ID NO:4. However, since the construction of chimeric (fusion) proteins constitutes a standard laboratory procedure used by those of skill in the art, the claimed chimeric (fusion) proteins constitute obvious variants of the disclosed protein.

Claims 13, 15-16 and 18-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Leffers et al. (EMBL Accession Number S45142, January, 13, 1995).

Leffers et al. disclose an isolated protein with an amino acid sequence substantially homologous to SEQ ID NO:2 (see page attached STIC search report). With regard to claim 17,

while the proteolytic activity of said proteins (fragments) was not explicitly disclosed, said activity is, absent of evidence to the contrary, an inherent property of the protein (fragment). Moreover, the disclosed protein constitutes a fragment (411 amino acids) of the protein of SEQ ID NO:2 (415 amino acids). Leffers et al. differs from the instant invention in that they don't explicitly disclose the use of said proteins and protein fragments in fusion (chimeric) proteins nor do they disclose an isolated protein containing SEQ ID NO:4. However, since the construction of chimeric (fusion) proteins constitutes a standard laboratory procedure used by those of skill in the art, the claimed chimeric (fusion) proteins constitute obvious variants of the disclosed protein.

Claims 13-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nagase et al. (DNA Research, Vol. 2, pages 37-43, 1995).

Nagase et al. disclose nucleic acids (cDNA) that encode for proteins with an amino acid sequence substantially homologous to SEQ ID NO:2 (see page attached STIC search report). With regard to claim 17, while the proteolytic activity of said proteins (fragments) was not explicitly disclosed, said activity is, absent of evidence to the contrary, an inherent property of the protein (fragment). Nagase et al. differs from the instant invention in that they don't explicitly disclose the claimed proteins or the use of said proteins and protein fragments in fusion (chimeric) proteins nor do they disclose an isolated protein containing SEQ ID NO:4. However, since the nucleic acid sequence was disclosed, it would have been obvious to one of skill in the art to produce said protein recombinantly. Moreover, since the construction of chimeric (fusion)

proteins constitutes a standard laboratory procedure used by those of skill in the art, the claimed chimeric (fusion) proteins constitute obvious variants of the disclosed protein.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A. Zeman whose telephone number is (703) 608-7991. The examiner can normally be reached on Monday- Thursday, 7am -5:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (703) 308-3909. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Robert A. Zeman
January 30, 2003